Treatment and Research, Cleveland Clinic, Cleveland, OH, USA, [4]Virginia Mason Medical Center, Seattle, WA, USA, [5]Biogen Idec Inc., Weston, MA, USA, [6]Department of Neurology, First Faculty of Medicine, Charles University in Prague, Prague, Czech Republic

OBJECTIVES: To report the effect of BG-12 (dimethyl fumarate) in reducing the number of relapses requiring intravenous (IV) steroids and multiple sclerosis (MS)-related hospitalizations from a pre-specified integrated analysis of DEFINE and CONFIRM, which was designed to estimate–more precisely–the therapeutic effect of BG-12 versus placebo. **METHODS:** Eligible patients were aged 18–55 years with relapsing–remitting MS (McDonald criteria) and an Expanded Disability Status Scale score of 0–5.0. Patients who received oral BG-12 240 mg twice (BID) or three times daily (TID) or placebo were included and the integrated analysis was to be conducted only if baseline characteristics and treatment effects were similar between the studies. Numbers of relapses requiring IV steroids and MS-related hospitalizations (tertiary endpoints in DEFINE and CONFIRM) were assessed. **RESULTS:** The integrated analysis included 769, 761, and 771 patients who received BG-12 BID, TID, and placebo, respectively. Baseline characteristics and treatment effects were generally similar between DEFINE and CONFIRM. There were significantly fewer relapses requiring steroids and MS-related hospitalizations in both BG-12 groups compared with placebo. BG-12 reduced the annualized rate of relapses requiring IV steroids by 48% (BID; rate ratio, 0.52 [95% confidence interval, 0.43–0.64]) and 50% (TID; 0.50 [0.41–0.61]) versus placebo (both p<0.0001) and reduced the annualized rate of MS-related hospitalizations by 34% (BID; 0.66 [0.47–0.92]; p=0.0146) and 47% (TID; 0.53 [0.37–0.75]; p=0.0004) at 2 years. **CONCLUSIONS:** BG-12 significantly reduced the number of relapses requiring IV steroids and MS-related hospitalizations, which suggests benefits with regard to patient burden and health economic savings due to decreased resource utilization. These findings further support the efficacy results of DEFINE and CONFIRM.

PND12

THE EFFICACY AND TOLERABILITY OF PERAMPANEL COMPARED TO OTHER ADJUNCTIVE RECENTLY APPROVED ANTI-EPILEPTIC DRUGS (AEDS) FOR THE TREATMENT OF REFRACTORY PARTIAL ONSET SEIZURES: A SYSTEMATIC REVIEW AND BAYESIAN NETWORK META-ANALYSIS (NMA)

Tongbram V[1], Khan N[1], Shah D[1], Fortier KJ[1], Hawkins N[2]

[1]*Oxford Outcomes, Morristown, NJ, USA,* [2]*Oxford Outcomes, Oxford, UK*

OBJECTIVES: Perampanel (PER) is the first orally active α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor antagonist approved for the adjunctive treatment of partial-onset seizures in patients with epilepsy aged 12 years and older. While the regulatory approval was on the basis of 3 RCTs, which demonstrated the efficacy and acceptable safety of perampanel relative to placebo, for the purpose of funding and health technology assessment decisions comparisons to other similar AED are necessary.The aim is to compare the clinical efficacy and tolerability of PER relative to other recently approved AEDs (lacosamide (LCM), retigabine (RTG), and eslicarbazepine (ESL)) for the adjunctive treatment of partial onset seizures with or without secondarily generalization. **METHODS:** A systematic literature review was conducted to identify all RCTs of PER and selected AEDs. EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials from 1998 to September 2011, abstracts from selected 2010 and 2011 conferences, reference lists of included studies and unpublished study reports were searched. The odds-ratio for three outcomes: “>50% reduction in seizure frequency”, “seizure freedom” and “withdrawal due to adverse events” were estimated using fixed- and random-effects Bayesian NMA models. **RESULTS:** Twelve RCTs (3 PER, 3 LCM, 3 RTG and 3 ESL) met the inclusion criteria. In the analysis for “>50% reduction in seizure frequency”, all AEDs performed significantly better than placebo with odds-ratio for PER being similar to the other comparators. In the analysis for “seizure freedom”, all AEDs except LCM performed significantly better than placebo. In the analysis for “withdrawal due to adverse events” PER had the lowest odds-ratio compared to other AEDs. No significant difference was observed in any of the three outcomes between PER and the other AEDs when compared against each other. **CONCLUSIONS:** Compared with other licensed adjunctive AEDs, perampanel offers similar clinical efficacy and tolerability profile.

PND13

CLINICAL AND NEURORADIOLOGICAL EFFECT OF BG-12 (DIMETHYL FUMARATE) IN SUBGROUPS OF PATIENTS WITH RELAPSING–REMITTING MULTIPLE SCLEROSIS (RRMS): AN INTEGRATED ANALYSIS OF THE PHASE 3 DEFINE AND CONFIRM STUDIES

Bar-Or A[1], Fox RJ[2], Gold R[3], Miller DH[4], Arnold DL[5], O'Gorman J[6], Yang M[6], Sheikh SI[6], Viglietta V[6], Dawson KT[6], Hutchinson M[7]

[1]*Montreal Neurological Institute and Hospital, Montreal, QC, Canada,* [2]*Mellen Center for Multiple Sclerosis Treatment and Research, Cleveland Clinic, Cleveland, OH, USA,* [3]*St Josef Hospital, Bochum, Germany,* [4]*University College London Institute of Neurology, London, UK,* [5]*Montreal Neurological Institute and Hospital; and NeuroRx Research, Montreal, QC, Canada,* [6]*Biogen Idec Inc., Weston, MA, USA,* [7]*St Vincent's University Hospital, Dublin, Ireland*

OBJECTIVES: To report efficacy of BG-12 (dimethyl fumarate) in pre-specified patient subgroups stratified by age, gender, treatment history, prior relapses, Expanded Disability Status Score (EDSS), McDonald criteria, T2 lesion volume, and presence/absence of gadolinium-enhancing lesions at baseline in a pre-specified integrated analysis of DEFINE and CONFIRM. This analysis was designed to estimate–more precisely–the treatment effect of BG-12 versus placebo. **METHODS:** Eligible patients were aged 18–55 years with a diagnosis of relapsing-remitting multiple sclerosis (RRMS) (McDonald criteria) and an EDSS score of 0–5.0. Patients receiving BG-12 240 mg twice (BID) or three times daily (TID) or placebo were included in this analysis. Primary endpoints were proportion of patients relapsed (DEFINE) and annualized relapse rate (ARR) (CONFIRM) at 2 years. Secondary endpoints included number of new/enlarging T2 lesions and disability progression. The pre-specified integrated analysis was to be conducted only if baseline characteristics and treatment effects were consistent between the studies. **RESULTS:** The integrated intent-to-treat population comprised 2,301 patients while MRI evaluations were performed in a cohort of 1,046 patients. Baseline characteristics and treatment effects were generally similar across studies. Both BG-12 BID and TID reduced ARR versus placebo at 2 years by approximately 50%, risk of relapse, number of new/enlarging T2 lesions, and risk of disability progression at 2 years versus placebo across the subgroups. For example, ARR versus placebo at 2 years was reduced by 50% (BID; rate ratio 0.50 [95% confidence interval 0.40–0.64]) and 53% (TID; 0.47 [0.37–0.60]) in patients with ≤1 relapse in the year before study entry and 47% (BID; 0.53 [0.40–0.72]) and 41% (TID; 0.59 [0.44–0.80]) in patients with ≥2 relapses. **CONCLUSIONS:** These findings further indicate consistent efficacy of BG-12 on both clinical and neuroradiological measures across a wide spectrum of RRMS patients.

PND14

PROPENSITY SCORE ANALYSIS IN MEPS 2003-2010: PCS AND MCS SCORES AFTER MIGRAINE TREATMENTS

Wu IH, Johnson ML, Aparasu RR

University of Houston, Houston, TX, USA

OBJECTIVES: Migraine is a public health problem that has an impact on both the individual sufferer and on society. The objective of this study was to examine the PCS (physical component summary) and MCS (mental component summary) score after being treated with one of the two different recommended level A medications – Triptans and Anti-epileptics. **METHODS:** MEPS data 2003-2010 (with panel 9-14) were downloaded from the AHRQ website. Migraine patients who started to receive either Triptans or Anti-epileptics in round 3 were retained in the cohort. Patients who received combination therapy or received the medication in round 1 or 2 were excluded in order to control for the baseline characteristics. Propensity score method was used to ensure the patients being compared are equal within each tertile. The predicted probability of receiving Triptans was calculated for all patients in the cohort by using multiple logistic regression to control for demographics, comorbidity and PCS/MCS in round 2. The probabilities were then stratified into tertiles. The outcomes – PCS and MCS in round 4 were compared within each tertile to examine if there were any differences between the two medications. **RESULTS:** Overall there were 120 patients in the cohort with weighted frequency of 2,779,074 (2,049,642 for Triptans and 729,432 for Anti-epileptics). After the propensity score stratification, all the baseline information between the two treatment cohorts were equal in each tertile except race in tertile 2 (p=0.0124). After the outcomes comparison, there were no differences in round 4 PCS and MCS score between the two medications for all three tertiles. **CONCLUSIONS:** Triptans are the most expensive among all the migraine medications. However, the findings of our study demonstrated there were no differences in PCS and MCS after the treatment. Future studies should examine different outcomes and see if Triptans can improve other clinical findings.

PND15

MULTIPLE SCLEROSIS EARLY TREATMENT RATES IN UNITED STATES VETERANS

Xie Y[1], Lafleur J[1], Kamauu A[2], Schuerch M[3], Foskett N[3], Nelson RE[1]

[1]*University of Utah, Salt Lake City, UT, USA,* [2]*Anolinx, LLC, Salt Lake City, UT, USA,* [3]*F. Hoffman-La Roche Ltd, Basel, Switzerland*

OBJECTIVES: Multiple sclerosis (MS) is a common autoimmune demyelinating disease of the central nervous system. Early treatment of MS aids in repressing the most severe stage of acute axonal injury. The objective of this study was to characterize the proportion of MS patients who received early treatment, defined as an immunosuppressive treatment within 12 months following diagnosis. **METHODS:** We identified patients with an MS diagnosis who sought care in the US Veterans Health Administration (VHA) system from 1999-2010. The index date was the date of firs MS diagnosis. Patients who did not have at least 12 months of follow-up time were excluded. Descriptive statistics were used to characterize prescriptions for medications commonly used to treat MS in the 12 months following the index date. **RESULTS:** Our analysis cohort consisted of 6,011 MS patients. Mean age was 53.8 (SD 13.4) years and 80.7% were male. Race was known in 40.8%; of which most were white (80.2%) or black (16.0%). Only 35.3% of MS patients had a prescription for MS treatment in the 12 months following the index date. The most common MS treatments among MS patients were interferon beta 1a (13.2%), glatiramer (10.3%), amantadine (6.9%), prednisone (6.5%), and methylprednisolone (5.5%). Younger patients were more likely to have prescriptions. In a subset of 3,312 patients age <55, e.g., those who would be eligible for a clinical trial, 44.1% had a prescription for any immunosuppressive therapy used to treat MS. Interferon beta 1a (17.9%) was the most common treatment in this subgroup followed by glatiramer (13.6%), amantadine (8.9%), methylprednisolone (7.3%), and prednisone (6.8%). **CONCLUSIONS:** This descriptive analysis indicates that most patients with a diagnosis of MS do not receive early immunosuppressive therapy. Future research should identify relevant barriers to treatment and potential solutions to overcoming these barriers.

PND16

ANTIEPILEPTIC DRUG SWITCHING AND THE RISK OF SEIZURE-RELATED EVENTS

Hansen RN[1], Nguyen HP[1], Sullivan SD[2]

[1]*University of Washington, Seattle, WA, USA,* [2]*University of Washington, Pharmaceutical Outcomes Research and Policy Program, Seattle, WA, USA*

OBJECTIVES: Older antiepileptic drugs (AEDs) are known to have a narrow therapeutic index. As a consequence, switching between bioequivalent AEDs remains controversial in the management of epilepsy. We investigated the association between A-rated switching of each class of currently available AED medication and emergent treatment for a seizure-related event. **METHODS:** We used a case-control method and claims data from the 2010-2011 Truven Health MarketScan® Commercial Claims Database to estimate the risk of seizure following a medication switch. Cases and controls with an epilepsy diagnosis were identified by emergency/inpatient or outpatient visit claims, respectively. Cases and controls (n=8,106) were matched 1:1 by age, seizure diagnosis category and seizure medication. The exposure was defined as a switch between A-rated AEDs during the 90 days prior to index date. Conditional logistic regression was used to estimate the association, adjusting for gender, baseline Deyo-Charlson Comorbidity Index (0, 1, 2, or 3+), region (Northeast, Central, South, and West), and total AED medications. **RESULTS:** A switch between A-rated AEDs occurred in 1053 (23.2%) cases and 818 (18.0%) matched controls. The unadjusted and adjusted odds ratios of a seizure-related event for switching were 1.39 (95% CI: 1.25-1.54) and 1.22 (95% CI: 1.10-1.37), respectively. The independent risk of an event also increased with each category increase in the Charlson score (CCI=1: 1.60, 95% CI: 1.42-1.81; CCI=2: 1.72, 95% CI: 1.44-2.06; CCI=3+: 3.42, 95% CI: 2.84-4.11). Older AED medications had infrequent switches compared to newer agents and were not associated with events. **CONCLUSIONS:** We found a modest association between AED switching and seizure-related events. Our analysis suggests that the behavior of switching alone may lead to seizure-related events regardless of the medication. Other disease or environmental characteristics may contribute to this association. Until more conclusive evidence is available, health care professionals and patients should undertake switching of bioequivalent AEDs on an individual basis.

PND17

STUDY OF PSEUDOBULBAR AFFECT SYMPTOMS IN VETERANS WITH MILD TRAUMATIC BRAIN INJURY

Fonda JR[1], McGlinchey RE[1], Milberg WP[1], Rudolph JL[1], Hunt PR[2], Reynolds MW[2], Yonan C[3]
[1]*VA Boston Healthcare System, Boston, MA, USA,* [2]*United BioSource Corporation, Inc., Lexington, MA, USA,* [3]*Avanir Pharmaceuticals, Inc., Grass Valley, CA, USA*

OBJECTIVES: Pseudobulbar affect (PBA) is a neurological syndrome characterized by disinhibition of emotional expression and can occur following traumatic brain injury (TBI). Service members returning from Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) have unprecedented risk for mild TBI (mTBI), primarily from exposure to blast-related munitions. The prevalence of PBA in OEF/OIF veterans with mTBI is unknown. This study will determine the prevalence of PBA symptoms in OEF/OIF veterans with mTBI and characterize the populations with mTBI and PBA symptoms. **METHODS***: Participants*: Veterans receiving health care from the VA in the New England region (VISN-1) who tested positive on the VA standard TBI screen, excluding those with a current diagnosis of bipolar disorder, schizophrenia or other psychotic disorder. *Procedure*: TBI-positive veterans will be mailed the Center for Neurologic Study-Lability Scale (CNS-LS) questionnaire, a tool to assess PBA symptoms, supplemented with a validation question "Have you ever experienced involuntary episodes of crying and/or laughing that were exaggerated or even contrary to how you felt at the time?" VA clinical data will be used to characterize the entire study population and subset that return the CNS-LS questionnaire. *Outcome*: Participants will screen positive for PBA symptoms with a CNS-LS score ≥ 13 and answering yes to the validation question. We will determine the prevalence and 95% confidence interval of positive screens in the study population. **RESULTS:** There were 4,951 OEF/OIF veterans in Massachusetts who completed the VA TBI screen between April 2007 and February 2012, of whom 1,051 (21%) tested positive. We are currently identifying our study sample and will have preliminary results at the time of the conference. **CONCLUSIONS:** Ultimately, we propose a more comprehensive examination of the nation's veterans with mTBI to determine the overall prevalence of PBA. Identifying individuals who may be at risk for PBA will have important social and health care implications.

NEUROLOGICAL DISORDERS – Cost Studies

PND18

A DESCRIPTIVE ANALYSIS OF DRUG ACQUISITION COSTS TO TREAT MULTIPLE SCLEROSIS (MS) IN BRAZIL: THE MINISTRY OF HEALTH (MOH) PERSPECTIVE

Alexandre RF, Mosca M, Schneiders RE, Zimmermann IR, do Nascimento Jr JM, Gadelha CA
Ministry of Health, Brasília, DF, Brazil

OBJECTIVES: The treatment of MS, relapsing-remitting or secondary-progressive forms, is available in the Brazilian public health system (SUS), according to guidelines of MoH. Here, we describe the profile of the MoH' financial resources applied on the acquisition of drugs to treat MS in 2011 and 2012. **METHODS:** Descriptive analysis of the expenses with drugs to treat MS where the MoH is responsible for their acquisition: beta-Interferon, glatiramer and natalizumab. The expenses were calculated based on the amount dispensed and acquisition prices in 2011 and 2012 (current values; exchange rate: US$ 1 = R$ 2.04), obtained from MoH databases. **RESULTS:** In 2011, the expenses of MoH with the acquisition of medicines for MS reached to US$ 144,323,965.92, representing 7.2% of its annual resources applied on the acquisition of high-cost medications. Of this amount, US$ 112,182,371.80 was destined to the beta-interferon (77.8%), US$ 30,383,351.47 to the glatiramer (21.2%) and US$ 1,758,242.65 to the natalizumab (1.0%). In 2012, these same expenses increased to US$ 184,985,919.97 (a 28.2% difference). Of this amount, 78.4% was destined to the beta-interferon, 17.9% to the glatiramer and 3.7% to the natalizumab (3.7%). During this period, there was a mean price reduction of 13.2% (8.0 to 18.4%) and a mean increase of 38.6% (18.4 to 110%) in the amount of medicines dispensed. **CONCLUSIONS:** The drugs used in MS have relevant impacts on the MoH' budget. Thus, strategies to optimize resources, as the centralized acquisition of these medicines, which occurs since 2010, provide systematic price reduction and allow larger availability of medicines.

PND19

ANNUAL HEALTH CARE COSTS AND UTILIZATION IN ADULTS TAKING LONG OR SHORT ACTING ANTIEPILEPTIC MONOTHERAPY

Cramer J[1], Wang Z[2], Chang E[3], Copher R[2], Cherepanov D[3], Broder M[3]
[1]*Yale University School of Medicine, Houston, TX, USA,* [2]*Eisai, Inc., Woodcliff Lake, NJ, USA,* [3]*Partnership for Health Analytic Research, LLC, Beverly Hills, CA, USA*

OBJECTIVES: Adherence to antiepileptic drugs (AEDs) is imperfect and AEDs of long half-life or duration of action (e.g., extended release) might mitigate the impact of missed doses. We compared costs and utilization between patients treated with long-acting (LA) and short-acting (SA) AED monotherapy. **METHODS:** A retrospective cohort analysis was conducted using claims data (OptumInsight). We included adult epilepsy patients (≥1 epilepsy diagnosis in 2010 and 2011) who used AED monotherapy and were continuously enrolled in 2011. Patients were excluded if they had <2 AED fills, <9 months of treatment, or a treatment gap >60 days. Based on published data and expert opinion, AEDs were classified as LA or SA. Pharmacy and medical claims in 2011 were used to determine costs and utilization. Claims associated with an epilepsy diagnosis, test, or AEDs were considered epilepsy-related. Baseline group differences were adjusted using multivariate analyses. **RESULTS:** The 4058 (49.6%) LA users and 4122 (50.4%) SA users were mean age: 47.7 versus 45.1 years, female: 47.6% versus 57.0%; and had epilepsy-specific comorbidities: 19% versus 25%, respectively; all P<0.001. Compared with SA users, LA users had lower mean overall costs ($9,757 vs. $12,689) and epilepsy-related costs ($3,539 vs. 5,279) and lower rate of overall (8.7% vs. 10.8%) and epilepsy-related hospitalization (5.7% vs. 7.5%) (all P<0.01). After adjusting for demographics, usual care physician, and comorbidities, mean overall costs were lower by $686 (P=0.137) and mean epilepsy-related costs by $894 (P=0.005) in LA users than in SA users. **CONCLUSIONS:** Patients with epilepsy treated with LA AED monotherapy incur a lower economic burden than those treated with SA AED monotherapy. This study indicates that using AEDs with more extended coverage between doses may decrease health care use and lower costs. Future studies should examine the impact of duration of action on outcomes in combination therapy and in adolescents.

PND20

ASSESSING DRUG COSTS FOR USE IN COMPARATIVE EFFECTIVENESS RESEARCH

Levy JF[1], Meek PD[2], Rosenberg MA[1], Vanness D[1], Farrell PM[1]
[1]*University of Wisconsin, Madison, WI, USA,* [2]*Albany College of Pharmacy and Health Sciences, Albany, NY, USA*

OBJECTIVES: Current procedures to assess costs of drugs for use in comparative effectiveness studies fail to account for important issues related to pharmacy practice such as availability of generic drugs, differing manufacturer and package sizes, and clinically equivalent and reasonably interchangeable dosages. This work proposes a method aimed at better estimation of drug costs that includes a level of uncertainty. **METHODS:** Using patient drug histories and the Micromedex Redbook costs database, we construct an algorithm which accurately matches every prescription drug order to the full set of therapeutically appropriate National Drug Codes (NDCs) that could be used to fill each prescription. The algorithm, calculated on a per unit of ingredient, is flexible and can be modified to include more or less inclusive sets of possible NDC codes based on various definitions of reasonably interchangeable drug formulations. We compare a (i) simple method, using only a single NDC code, (ii) complete method that matches every potentially suitable NDC code, and (iii) pill rationing to favor exact doses. The complete and pill rationing methods introduce uncertainty between what was prescribed and what NDC code could be used to fill each prescription. **RESULTS:** As a concrete example using 500mg dose of Cephalexin, our simple method yields an estimated cost of $2.74 per dose, our complete method with 556 NDCs yielded mean (sd) $3.61 (2.40), and pill rationing with 314 NDCs yielded mean (sd) $3.55 (1.73). **CONCLUSIONS:** This method highlights several important issues when assessing costs of a drug included in comparative effectiveness studies. It also proposes a way to better account for uncertainty when modeling estimated costs and more consistency in including individuals using the same drug dosage at the same cost.

PND21

ECONOMIC BURDEN OF ADVERSE TREATMENT EFFECTS IN PARKINSON'S DISEASE: EVIDENCE FROM A LARGE EMPLOYER POPULATION

Davis KL[1], Fitzgerald TP[2], Meyers J[1], Kulkarni A[2], Svarvar P[2], Hewitt DJ[2]
[1]*RTI Health Solutions, Research Triangle Park, NC, USA,* [2]*Merck & Co., Inc., Whitehouse Station, NJ, USA*

OBJECTIVES: To assess increased all-cause costs incurred by patients experiencing various adverse effects (AEs) associated with Parkinson's disease (PD) and its treatments in a large, real-world population. **METHODS:** A retrospective analysis was conducted using the MarketScan database, an employer-based source of inpatient, outpatient, and pharmacy claims of >30 million lives from 2000–2011. Inclusion criteria were: ≥1 PD diagnosis (ICD-9-CM 332.0) and ≥1 anti-PD treatment claim (levodopa, dopamine agonist, anticholinergic, MAOB-inhibitor, COMT-inhibitor, or amantadine) during 2000-2011. Separate case/control cohort analyses were conducted for each AE (dyskinesia, orthostatic hypotension, secondary hypertension, nausea, edema,